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An Overview on the 10 Cellular Hallmarks of Cancer

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Abstract: ***Cancer is considered as one of the most fatal disease and a major issue that threatening the whole world because of the increasing number of affected people and its impact on the society. It is one of the major challenges that scientists face today, from a long time they are researching and doing trials which helps to fight this disease and to find a cure. The hallmarks of cancer help us in better understanding of cancer's common trait and in designing proper drugs for the treatment. In this article we will discuss how hallmarks of cancer help to develop targeted therapies and how it improves survival rate of patients.***

Keywords: Cancer, Hallmarks of cancer, Tumor cells

1. Introduction

There are six biological abilities that are characteristic of cancer, symptoms of, or acquired in the course of the multi-stage development of human tumours. These functions form an important basis for rationalizing the complexities of cancer treatment. This includes the maintenance of the proliferative signalling, evasion of growth inhibition, resistance to cell death, replicative immortality, induction of angiogenesis, and activation of invasion and metastasis. Based on these symptoms, the stability of the genome, giving rise to the diversity of a genetic disease, which speeds up their development, and inflammation, which contributes to the more characteristic features. The theoretical advances of the past decade, it has been added to the list of new features, from a prospective, community-reprogramming the body's metabolism and energy consumption, the avoidance of the immune system deterioration. In addition to cancer cells, tumours exhibit another of complexity: they contain a set of word of mouth, most of the normal cells that contribute to the acquisition of things, and the creation of a "tumour microenvironment". "To the memory of the widespread use of these concepts will increasingly affect the development of a new human cancer treatments.

2. Cellular Hallmarks of Cancer

Hallmark Number 1: Replicative Immortality

Normal human cells have the ultimate ability to undergo mitosis, which is well-known because there is a problem with the absence of replication. This is often largely due partially to the telomeres of the chromosomes, which are the ends of the chromosomes that get shorter after each mitotic division[1]. One of the primary people to look at this was Leonard Hayflick. And when cells stop dividing, they're known to own reached Hayflick's limit. And once cells reach Hayflick's limit, they'll not divide they enter the G0 phase of the cell cycle, also called cellular senescence. In normal cells, they'll stop dividing once the telomeres become too short. However, an indicator of cancer cells is that they will greatly exceed what's called Hayflick's limit and still undergo mitosis [1]. Cancer cells can greatly exceed Hayflick's limit by using an enzyme mentioned as telomerase. Telomerase can elongate telomeres after they get too short to sustain proliferation. This enzyme is seen in great amounts in different cancer types. By cancer cells being immortal, they'll continuously proliferate, and they'll transfer genes to daughter cells that are mutated. This leads us to hallmark number two of cancer observed as genome instability.

Hallmark Number 2: Genome Instability

In normal eukaryotic cells, they bear 22 autosomes and one pair of sex chromosomes that reside within the nucleus [2]. In an exceedingly normal cell undergoing DNA synthesis during the cell cycle, if it detects a mutation, which occurs within the gap phases of the cell cycle, the cell stops the cell cycle then repairs the mutation and re-enter the cell cycle [3]. Then the genes that are involved stopping the cell cycle from mutation is detected, known as tumour suppressors genes. However, cancer cells differ from normal cells because of their ability involves an abnormal number of chromosomes within the nucleus and also, they're going to be ready to undergo mitosis. Genes that are mutated in cancer or lost in cancer contribute to genome instability. These are called tumour gene suppressants. Conversely, some genes become overexpressed or mutationally activated and these are called oncogenes. These genes cause cells to proliferate uncontrollably. Notable genetic alterations that occur in cancer, especially to oncogenes similarly as tumour suppressor genes, are point mutations, deletion of chromosomes where tumour suppressor genes lie, also as loss of heterozygosity, and a number of other mutations and modifications.

Hallmark Number 3: Evasion of Growth Suppressor Signals

Mitosis in normal cells can be a tightly controlled process in which pro- and anti-proliferation signals combine cell function at the cell cycle level. In particular the G1 phase of the cell cycle can be an important test site where anti-growth signals contribute to cell proliferation [4]. However, due to

hallmark number two, genomic instability, most cancer cells can circumvent normal growth suppressor signals within the G1checkpoint to still proliferate. Cancer cells can evade growth suppressor signals with the tumour suppressor called retinoblastoma [3].Cancer cells with modified Rb remove this portrait or further cell proliferation. Rb is active suppressor, blocking the passage of cells through the restricted area in the G1 phase of the cell cycle. Another tumour suppressor called p53 is lost in many cancer types. This allows the cell cycle to progress despite DNA damage and other cellular stresses which may kill a conventional cell. With these gatekeeper genes are lost or mutated, cancer cells can sustain proliferation and resist cellular death.

Hallmark Number 4: Resistance to Apoptosis

Normal cells can initiate apoptosis in response to an abundance of DNA damage, DNA mutations, as well as other cellular stresses from external factors [3]. We all know that a neoplastic cell can still cycle through the cell cycle while bearing such DNA damage in other cellular stresses. Cancer cells are ready to resist death of cell by up-regulating pro-survival proteins to avoid necrobiosis within the presence of those stresses. One example of a pro-survival protein that's seen over expressed in many cancer types is that the pro-survival protein Bcl-2. Bcl-2 has anti-apoptotic relations like Bcl-2, Bcl-XL, Mcl-1, CED-9, A1, Bfl-1, and also pro-apoptotic relations like Bax, Bak, Bcl-Xs, Bim, and lots of others. In many cancer types, we see Bcl-XL and Bcl-2 relations particularly over-expressed.

Hallmark Number 5: Sustained Proliferation

Because cancer cells can resist death, they're going to sustain proliferation. With all the previous hallmarks, they'll try this quite easily. Within normal cells, protein signalling is additionally tightly controlled for tissue homeostasis and other cellular functions. Cancer cells are very different which they need the ability to proliferate as mentioned in Hallmarks 1 to 4 with loss of too many suppressor genes, also as over expression of oncogenes, like RAS, SARK, and plenty of others. Cancer cells even have the facility to stimulate the normal cells that surround them in which is known as the tumour microenvironment which provide them with essential growth factors. One protein that's well studied in cancer research is epidermal protein. The epidermal protein can bind to the receptor, which is expressed on cancer cells said as EGFR, to activate an oncogene well-studied in cancer research called RAS. RAS can have a plethora of downstream effects that positively regulate the cell proliferation of cancer cells.

Hallmark Number 6: Altered Metabolism

One of the key ways a neoplastic cell differs from a traditional cell is its metabolism. This reorganization of the metabolism is an emerging hallmark in cancer cells. For cancer cells to multiply uncontrollably, they need to make changes in their production of energy. Cancer cells achieve this by looking for and by using alternative sources and also alternate pathways of metabolism. Normal cells typically break down glucose during a process called glycolysis and convert it to pyruvate, which provides ATP, for the cell. This can be often largely happening within the mitochondria. However, different cancer cells convert sugar into lactate regardless of oxygen. Molecular cancer research also reveals several activating mutations and enzymes that help intensify this process. This allows cancer cells to convert metabolites through beneficial anabolic processes such as mitosis. Once we compare neoplastic cell metabolism to an average cell metabolism, we are going to see that an average cell takes in glucose, breaks it down by glycolysis to pyruvate and mitochondria undergoes the Krebs cycle which produces 36 ATP molecules in CO2, whereas a neoplastic cell undergoes aerobic glycolysis, produces low ATP and lactate which is important for cell proliferation and biomass incorporation.

Hallmark Number 7: Avoiding Immune Destruction

This is another emerging hallmark that permits cancer cells to be healthier and to survive within the host. The system consists of the many biological structures and processes that help humans to shield themselves against disease. For the right function the system should detect a large variation of various agents from viruses and parasitic worms to differentiate healthy tissue from foreign tissue. The organs of the system are identified as the thymus, lymph nodes, spleen, appendix, bone marrow, and lymphatic vesicles. Several cells are produced by each of those organs. Lymph nodes produce T cells which are matured within the thymus. Myeloid cells become macrophages which they're produced largely in every organ within the body. Dendritic cells and B cells produce antibodies and secretes cytokines. All of these cells are very important in protecting the host from outside invaders. Avoiding immune destruction that awake the system and destroys viruses in other foreign cell types within the frame. Cells of the system that engulf and destroy foreign particles are B cells, T lymphocytes or T cells, macrophages, and natural killer cells. However, cancer cells can protect themselves from invasion by T cells and other cell types by replenishing a well-studied protein in cancer biology called programmed-death-ligand 1. Programmed death-ligand, these proteins are transmembrane meaning that they're extracellular and intracellular. They play an important role in suppressing the system. Usually, the system responds to foreign antigens as foreign cells cause an increase in CD8 T specific antigen cells. T cells produce PD-1 and when they interact with PD L1 it is a test site to tell T cells to block the proliferation of immune defences. Cancer cells are highly intelligent when they regulate PD L1, which interacts with PD-1 so T cells cannot attack them [5]. This is usually the key to how tumour cells can protect the system

Hallmark Number 8: Tumor-Promoting Inflammation

The tumour microenvironment is commonly infiltrated with adaptive immune cells that enable tumours to mimic inflammatory conditions that are seen in normal tissues. Inflammation is seen within the early stages of several neoplastic diseases. Early inflammation can release chemicals into the tumour microenvironment which will result in mutations, and enable cells to accelerate the formation of the tumour. Moreover, they will undergo what is called epithelial to mesenchymal change, or EMT, and invade. Immune cells secrete cytokines. Cytokines regulate immune cell proliferation and accumulation. These cells secrete proteases, which are degrading enzymes that may break down proteins found within the extracellular matrix. Cancer cells can also secrete factors like chemokines to

immune cells. And immune cells can secrete these factors back to cancer cells which results in increases in cellular motility, cell movement, cellular survival, and a process called angiogenesis. All of this allows tumour cells to grow and survive and invade.

Hallmark Number 9: Induction of Angiogenesis

Angiogenesis is that the formation of latest blood vessels which is critical for sustained tumour growth and subsequent metastasis. All tumour cells require a blood supply to grow into an enormous size. Cancer cells can do that by using pro-angiogenic factors like vascular endothelial protein, also called VEGF to become activated in tumour cells and signal to epithelial cells to grow in order that a replacement vessel is formed. Immune infiltrating cells like macrophages can also secrete VEGF to induce angiogenesis. Persistent angiogenesis enables tumour expansion and native invasion through the delivery of oxygen and nutrients and also the production of growth factors that largely benefit tumour cells. Tumour cells grows farther far away from the blood vessels than the other cells because they need a faster rate of growth comparatively and so needs more oxygen. So new blood vessels form from already existing blood vessels and reach the tumour cells. This may continue because the tumour grows larger. Because this process isn't natural, these new blood vessels are often poorly made and are leaky and that they do not have strong integrity. This becomes easy for tumour cells to urge into and to urge out of them. This provides an outlet largely for tumour cells to urge into the bloodstream and also the lymphatics, and metastasize to distant sites.

Hallmark Number10: Activation of Invasion and Metastasis

Several things occur before we get a metastatic lesion in several cancer types. These steps are:

1) Cell to cell and cell-extracellular matrix interactions are altered.
2) Changes or loss of structural proteins that keep cells guaranteed to the extracellular matrix, which are integrins and other adhesion proteins.
3) There may be a loss of genes or mutation of genes that are seen in metastatic lesions called metastasis suppressor genes they're different from tumour suppressor genes. Once these genes are lost metastasis happens.
4) Recruitment of immune cells.
5) Epithelial-to-mesenchymal transition. Normal cells are cuboidal and stationary, absolute to the extracellular matrix by integrins and other adhesion molecules and that they are guaranteed to one another by E-cadherin and other cell-to-cell junctions. Loss happens over over-time the cell incorporates a gain of Mesenchymal proteins so change or loss in integrin adhesion to the extracellular matrix happens. This causes the cells to be more stretched and to function quite differently than a standard cell would. These cells become more invasive and begin to invade or enter surrounding tissues.

3. Conclusion

In conclusion, it has been made clear that THE HALLMARKS OF CANCERS are the main six biological capabilities acquired during the development of cancer cells. It has been then increased into eight capabilities and two enabling capabilities. These hallmarks have an essential role in rationalizing the severity of several diseases which cause due to the abnormal growth of cells in the body.

In comparison with a healthy cell and a cancer cell, the healthy functioning cell will find any DNA damages that the cell has. After detection a tumor suppressor gene p53 will cease all the cycling activities of the cell. It will then repair the DNA and allowed to go back in to the normal cell cycle. If the damage is so adequate the cell will go into a programmed cell death called apoptosis. The dead cells were removed by phagocytes and this will finally result into homeostasis (cellular and tissue level). In cancer cells the p53 repressor gene is either absent or mutated as a result it cannot function properly if any DNA damage is detected. The cell cycle will continue and the defected cells never undergo apoptosis. There rise a genomic instability and this instability will produce a daughter cell with the mutation. This mutated cell will give rise to other daughter cells and so on. This results in the formation of a hyperplastic legion that can be seen in several adenocarcinomas. Finally, the body will develop cancer in situ followed by inflammation, loss of immune system and lack of cell death. Now the body has invasive cancer that will move from the organ of its origin to other organs.

The hallmarks of cancer give us a very good opportunity to understand what goes wrong in a cancer cell, which helps in development and provide new way to treat human cancer.

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